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Bipolar disorder traits: An electroencephalogram systematic review

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Abstract:

Bipolar disorder (BD) is a serious mental disorder that globally affected 40 million people in 2019. According to the National Alliance on Mental Illness (NAMI), the present state of scientific knowledge only permits psychiatrists to diagnose BD using subjective and imprecise questionnaires. Therefore, developing a diagnostic tool with objective and precise biomarkers should be a major focus of research in this field. Among the potential biomarkers for BD, electroencephalogram (EEG)-based signatures of BD are considered to be the most optimal marker due to their strong links with behavioural symptoms and also their non-invasiveness. The goal of this review is to give a detailed summary of current techniques for investigating the traces of BD through EEG abnormalities. In this review, 13 studies from databases such as ScienceDirect and PubMed seeking to utilize EEG characteristics to diagnose BD were selected. The search keywords were "EEG in BD diagnosis", "EEG microstates in BD", and "EEG features for BD patients". The publication date was set from 2007 to 2021. From these studies, we synthesize the effects of BD on each EEG feature, as well as detail the pros and cons when using each feature as a biomarker for BD. Results showed that EEG microstates demonstrate their potential among the seven EEG properties discussed in this article, as shown by several studies. By definition, EEG microstates are a dynamic representation of the spatial distribution of the scalp's electric potential as it varies over time. Specifically, four microstate classes recorded in different brain regions are classified into A (right-frontal left-posterior), B (left-frontal right-posterior), C (midline frontal-occipital), and D (midline frontal topographies). Greater presence of microstate class B in BD patients during task-free resting states are a distinctive characteristic of BD patients from which BD can be differentiated from other psychiatric illnesses. Besides microstates, EEG resting states are also considered to have a bright future in BD diagnosis. Specifically, by investigating brain frequency bands, researchers have discovered that BD patients exhibit abnormal delta and alpha signals as compared to healthy controls (HCs). The abnormalities of microstate B in EEG microstate characteristics would be the most promising biomarker for detecting BD. In addition, anomalies in delta and alpha signals during resting EEG states are possible BD diagnostic indicators.

Keywords: **bipolar disorder, EEG diagnosis, EEG features.**

Classification number: **3.6**

Introduction

BD is a severe mental disorder that afflicted 40 million individuals globally in 2019. BD is defined as a brain condition that causes a person to experience significant changes in emotions, mood, and energy levels ranging from extremely low to extremely high [1]. Life is split into two realities for the many millions of people who suffer from bipolar illness across the world: mania and depression. BD is divided into three typical types, although there are numerous variations.

Bipolar type I is defined as a person who has manic episodes or signs of manic episodes for at least seven days [1]. Bipolar type I individuas may necessitate emergency hospitalization in some situations. Depressive episodes have also been known to last for at least two weeks. In addition, bipolar type II is defined as a sequence of depressed and hypomanic episodes rather than the full-blown manic episodes as seen in BD type I. Finally, cyclothymia, another form of BD, is defined as a mood disorder

BD typical symptoms

As mentioned before, bipolar patients mainly suffer from two distinctive phases:

Phase 1: Depression period

During the depression period, patients likely experience:

+ Lack of motivation, energy
+ Irritability
+ Feeling negative about everything
+ Suicidal thoughts
+ Insomnia, lack of appetite
+ Delusion, hallucination, and illogical thinking are discovered in emergency cases

Phase 2: Maniac period

During the maniac period, patients likely suffer from:

+ Overly happy, elated
+ Feeling irritated and agitated
+ Spending significant sums of money on expensive and, at times, unaffordable objects is an example of conduct that frequently has negative outcomes.
+ Making decisions or speaking things that others perceive as hazardous or damaging and that are out of character
+ Insomnia, lack of appetite

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in which sufferers experience hypomania and mild depression (at least for two years). People with cyclothymia find it difficult to find a good balance in their lifestyles [1].

According to NAMI, a physician may perform a physical examination, conduct an interview, and request laboratory testing to diagnose BD [2]. While a blood test or body scan cannot detect BD, they may help rule out other disorders that might mimic it, such as hyperthyroidism [3]. Therefore, developing a diagnostic tool with a greater scientific basis is the main target of this research with the understanding that EEG can be applied to diagnose BD and especially to distinguish BD from other serious psychiatric disorders such as schizophrenia (SCH). Realistically speaking, EEG is a diagnostic tool that is used to record electrical activity in the brain. By using small, metal electrodes attached to the scalp, EEG can record the electrical impulses that are communicated by our brain cells and display them as wavy lines on an EEG recording [4].

In neuro-engineering, EEG has been widely used to detect many serious brain disorders such as epilepsy, SCH, and so on [4]. To the best of the authors' knowledge, despite being applied in diagnosing many psychiatric disorders, there is not much research about using EEG as a diagnostic tool to detect BD. Traditionally, to diagnose BD, the results are mainly dependent on patient reports, which are subjective [5]. Therefore, this study aims to fulfil that missing piece by focusing on using EEG signals to detect and classify BD with other disorders. Therefore, in this review, the cognitive and affective changes in BD patients are meticulously discussed. Based on those abnormalities, studies about utilizing EEG features in diagnosing BD will be presented in a systematic way. Moreover, this review also suggests the most optimal solution for the diagnosis.

Paper selection criteria

Fifty papers were selected from academically trusted scientific library sources such as PubMed and ScienceDirect. After analysing all articles, only 13 papers fit all criteria (listed below) and were utilized for this review. In the scope of this review, the literature contains several articles with focus on specific biomarkers, literature reviews, or computational methods for BD diagnosis. This review is structured by the cognitive and affective changes in BD patients, followed by a brief explanation of EEG features to diagnose BD based on these changes. Finally, the research topics will be presented as well as some research constraints.

Included criteria: All research papers applied the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) as the standard subject recruitment criterion. Selected papers must be authored by credentialed professionals or reliable sources. In addition, researchers must provide precise results with a justifiable explanation.

Excluded criteria: After vetting the papers with multiple online sources, papers that only give hypotheses and do not have convincing arguments will be rejected. Besides that, papers that were published before 2,000 were also excluded to maintain the applicability of this review.

BD cognitive and affective changes

BD exemplifies the notion of mood and affect. Numerous studies suggest that bipolar illness may be associated with the disturbance of the brain or other bodily functions [3]. However, no distinct theoretical standpoint has been established. However, the viewpoint of applying EEG in psychiatry as an alternative to the DSM for understanding and treating people with mental disorders has been mentioned. This method is commonly used by healthcare professionals for the treatment and education of individuals with mental problems. BD patients often encounter physiologic alterations. Hence, in our review, all of the main findings about the cognitive and affective alterations in BD patients are summarized in Fig. 1 below:

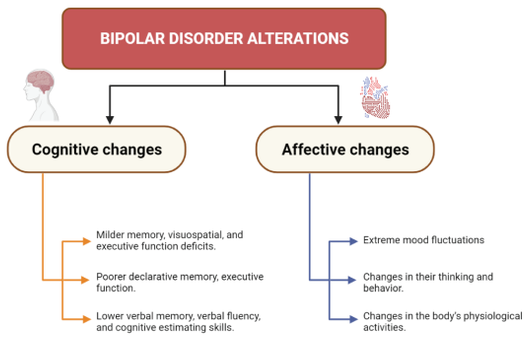

Fig. 1. A summary of behavioural changes in BD patients in terms of cognitive and affective functions.

Cognitive changes

The mental processes that allow us to receive, assess, store, process, develop, and recover knowledge gained from external stimuli are referred to as brain cognitive functions. This process improves our capacity to grasp and relate to the world. Cognitive alterations have been widely observed in bipolar patients [3]. Many studies have been carried out that describe as well as explain these abnormal changes. These changes can be typically listed as:

Milder memory, visuospatial, and executive function deficits: Although BD patients perform numerically better than patients with SCH in terms of neurocognitive performance, bipolar adults demonstrate the same qualitative impairment pattern in both diseases. Specifically, studies indicate that some individuals with BD have also complained of memory impairment during periods of elevated and depressed emotions, as well as at other times. As a person's mood changes, they may also experience memory alterations. Therefore, memory issues might worsen when an individual's mood grows more intense [3]. Moreover, many studies have shown that unaffected relatives and children of bipolar patients exhibit mild memory, visuospatial, and executive function deficits [3]. Specifically, endophenotype biomarkers have indicated that BD is commonly inherited, with genetic factors accounting for around 80% of the disease's causes.

Bipolar depression is the most common mental condition that is handed down from generation to generation. If one parent has BD, their child has a 10% risk of developing the disease.

Poorer decision-making and declarative memory: When compared to HCs, bipolar patients display psychomotor retardation as well as poor declarative memory, decision-making, and, to a lesser extent, visual memory, and attention [3]. Scientists discovered that alterations in the brain cause memory issues in certain individuals with BD. Alteration in the prefrontal cortex can be damaging as it is involved in planning, attention, problem-solving, and memory, among other tasks [2].

Lower verbal memory, verbal fluency, and cognitive estimating skills: A study has shown that when compared to depressed and remitted patients, bipolar patients exhibit lower verbal memory, verbal fluency, and cognitive estimating skills [3]. The study also indicated that the primary symptom of bipolar depression is a loss of verbal memory. Moreover, another research showed that manic episodes were associated with more severe deficiencies in verbal and working memory, executive function/reasoning, and problem-solving [6].

Therefore, several research studies have revealed that bipolar individuals, regardless of their stage of disease, exhibit cognitive deficiencies. At the time of their release from an inpatient facility, BD patients were shown to have a worse cognitive profile than depressive patients in terms of psychomotor slowness and selective attention in one study [7]. Conspicuously, the examination of the same group of participants six to eight weeks after release found that manic patients had retained the same pattern of impaired psychomotor speed and a high tendency for the perseverative behaviours that they exhibited at the time of discharge [7].

Affective changes

Fear, pleasure, the satisfaction of all sorts, sexuality, and jealousy are among the brain activities related to emotions [8]. Affective functions are situated in the brain's most fundamental areas, particularly the limbic region, which we share with many other animals [8]. In bipolar individuals, affective functioning alterations are different among the disorder's phases. For most BD patients, these changes can be typically listed as:

Extreme mood fluctuations: A person suffering from depression or mania may experience extreme mood fluctuations (also known as mood swings). Mood fluctuations may catch them off guard at first. However, BD patients may notice trends or symptoms that they are approaching a phase of mania or depression over time since the patterns of mood fluctuations mainly depend on the type of BD [8].

Changes in their thinking and behaviour: In most cases, BD patients exhibit changes in their thinking and behaviour. Frequently, BD individuals may exhibit pressurized speech and racing thoughts during manic episodes. In some cases, patients with BD are delusive in certain critical circumstances. For instance, they may believe that they have supernatural powers. In addition, bipolar individuals also experience depressed episodes along with euphoric moods, which are comparable to major depressive disorder (so-called unipolar depression) [8].

Changes in the body's physiological activities

Aside from changes in mood, BD patients are also observed to have changes in their physiological activities. Many studies have pointed out some typical lifestyle changes observed in manic patients that could be the result of physiological changes. For instance, in a study on women with mental disorders [9], in the instance BD, women are more likely to engage in reckless sexual conduct. In another study, researchers studied 63 female outpatients with a diagnosis of bipolar illness from the bipolar program at Favaloro University [10]. The remaining 63 women had no psychiatric history and maintained a healthy lifestyle. The 63 bipolar women were not in committed monogamous partnerships and engaged in casual sexual activity. They also had personal relationships with people whose HIV or other sexually transmitted illness status were unknown. In addition, they were infected with two or more sexually transmitted diseases. The authors determined that women with bipolar illness were more prone than healthy women (women without BD) to engage in hazardous and promiscuous conduct [10]. According to the American Psychiatric Association, BD is characterized by fundamental sleep disturbances. The diagnostic criteria also imply that during manic periods there may be a decreased demand for sleep, but during depressive episodes, insomnia or hypersomnia may occur virtually every day.

The physiological alterations of BD patients are explained in Table 1.

Table 1. Physiological changes in BD patients.

Physiological changes in BD patients	
Sleep pattern	People with bipolar illness report lower-quality sleep in general between cycles, including increased night waking, an overall impression of less sleep, and occasional insomnia.
Energy level	Sleep difficulties are connected to lower energy levels and, as a result, a lower probability of engaging in healthy habits in people with bipolar (e.g., socializing, shopping, cooking, and exercising).
Alcohol and drug use	Self-medicating with drugs and alcohol is prevalent among individuals with BD. At first, these medications appear to alleviate the symptoms of manic and depressive episodes, which explains why so many people with bipolar illnesses become addicted.
Sex drive	Sexual activities may be affected by the illness. Patients may suffer from hypersexuality during a manic episode. This might put them at a greater risk of harmful activities, such as developing a sexually transmitted infection (STI).

EEG biomarkers in BD diagnosis

EEG microstates

What are EEG microstates? EEG microstates are fleeting, or quasi-stable, patterned states [8]. These microstates typically last between milliseconds and seconds and represent the most fundamental manifestations of human brain processes; they are hence dubbed "the atoms of cognition". Initially, microstates

estimations and analysis were performed using alpha-band activity, but nowadays, wider bandwidth EEG bands are commonly used. Due to the quasi-stability of microstates, global EEG topography is stable, but intensity and polarity may fluctuate [11].

How is an EEG microstate obtained? In one observational study, researchers aimed to apply electroencephalographic microstates to classify SCH and BD [11]. Twenty SCH patients (mean age 25.2±6.8, n=15 females), thirty-four BD patients (mean age 22.8±4.12, 13 female), and thirty-five HCs (mean age 24.9±6.2, n=25 females) were recruited. EEG data of the patients were recorded for 3 min at a resting state while they closed their eyes and sat on a chair comfortably. Fig. 2 illustrates the process of EEG data collection and processing. Specifically, data were acquired using a 64-channel device (Brain Product) and sampled at 5,000 Hz. The impedances were maintained under 5 Kohm. MATLAB 2013b and the MATLAB EEGLAB toolbox were employed to pre-process the data. A 48-52 Hz Parks-McClellan stop-band notch filter was employed to reduce electric interference from the 50 Hz line. Then, the data were band-pass filtered (0.1-40 Hz) and downsampled to 250 Hz. The data then were segmented into epochs of 2 s and poor epochs were discarded with evident muscle activation after being verified visually. Besides this, the researchers also employed independent component analysis (ICA) to eliminate the oculomotor component when necessary. Finally, the data were referred to as the average reference and bandpass filtered to 2-20 Hz. Microstate analysis was performed using MATLAB 2013b. Figure 3 depicts the four microstate classes for SCH patients, BD patients, and HCs. The 4 microstate classes explained 76.2, 74.1, and 76.0 percent of the global variation in SCH, BD, and HC patients, respectively, while one-way ANOVA revealed no significant differences (p=0.126) between SCH, BD, and HC patients. To exclude the effect of the varied template maps in different epochs, the global field power (GFP) of the EEG data was estimated for each participant with the longest length. In the first stage, all GFP peaks from all participants were clustered to generate the template maps. In the second step, all GFP peaks from the first step were clustered to identify which class each subject's template maps at each time point belonged to. When clustering, the modified k-means method with k restricted to 100 was utilized. In order to maintain continuity with earlier investigations, the EEG data were separated into four microstate topographies. The goal of this study is to analyse the four EEG microstates; we acquire four typical microstates for three distinct groups and all participants, independent of their medical condition. Across all groups, a global segmentation was performed, and one set of template maps was fitted to the initial data. These four all-group template maps as shown in Fig. 3 were then utilized to derive the microstate properties. Based on the microstate transition, the chance of transition between every two microstates back and forth was estimated. Twelve observed possible transitions were considered [11].

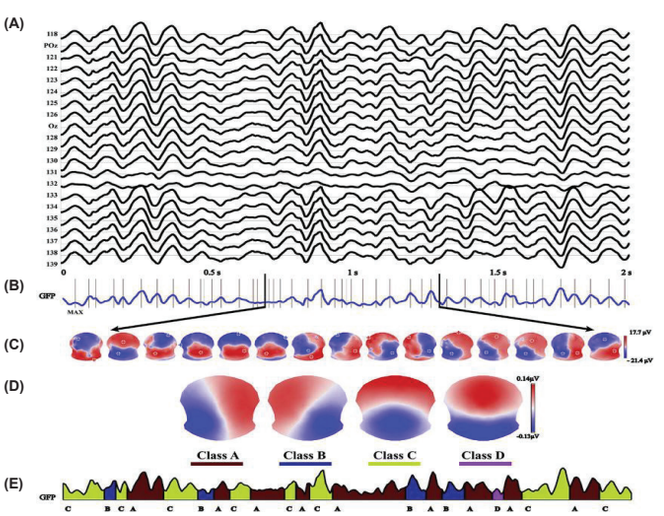

Fig. 2. A illustration of the EEG microstate data collection and processing [9].

EEG microstates in BD: As mentioned before, EEG microstates are considered one of the most state-of-the-art techniques in diagnosing many serious psychiatric disorders. In some studies, this even alters the conventional questionnaire diagnostic tools. Although many psychological studies have been conducted to diagnose SCH, few studies use this innovative technique to distinguish BD from other psychiatric disorders. According to a study, the researchers investigated the microstate features of EEG in patients with SCH, BD, and HCs to give an electro-directional physiological explanation and any mutual mechanism for the observed brain dysfunction of SCH and BD [11]. Another study, employed EEG microstates to investigate any potential resting state temporal dynamics abnormalities in BD. The findings are stated in Fig. 3 [12].

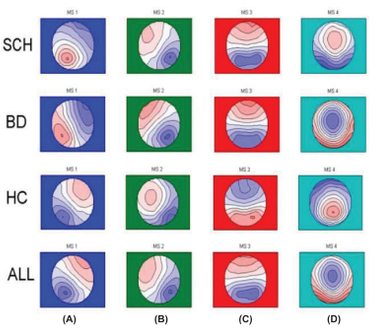

Fig. 3. EEG microstates (A, B, C, D) in SCH, BD, HCs, and ALL for all types of subjects [8].

EEG microstate data were transformed into four types of microstate topographies (A, B, C, D). From the experimental results, the authors concluded that BD patients exhibited a greater presence of microstates A compared to that of SCH [11]. Regarding microstates B, BD patients exhibit a greater presence of those microstates than that of SCH [11], and a reduced presence of microstates B in BD compared to HCs [12]. BD patients displayed less presence of microstates C than that of SCH [11]. Finally, BD patients displayed a greater presence of microstates D than that of SCH [8]. Table 2 illustrates all the findings from [11] and [13].

As can be seen from Table 2, bipolar patients exhibit greater frequent switching between microstates A and C, D and vice versa compared to SCH patients. Therefore, in clinical practice, microstate analysis can play a crucial role in diagnosing patients more accurately and treating them properly.

Table 2. EEG microstate findings summary in BD and SCH.

Microstate	BD	SCH
 A	BD patients exhibit a greater presence of microstate class A [11].	SCH exhibits less presence of microstate classes A and B [13].
 B	BD patients exhibit a greater presence of microstate class B [8]. However, when compared to HCs, BD patients indicated a reduction in microstate B [13].	
 C	BD patients exhibit less presence of microstate class C compared to the SCH group [11].	SCH patients indicate a greater presence of microstate class C and class D compared to the BD group [11].
 D	BD patients exhibit less presence of microstate class D compared to the SCH group [11].	

EEG resting states

What are EEG resting states? Recently, neuroimaging technologies have emerged as crucial tools for evaluating the brain status of individuals with consciousness issues (DOC). The recording and analysis of resting-state EEG have been extensively used by physicians owing to their comparatively cheap cost and portability [13]. EEG represents the electrical activity of the underlying neurons and includes information on neuronal population oscillations, the channel of information flow, and brain activity networks. Several characteristics obtained from EEG signal processing techniques have been presented to characterize the electrical properties of the brain with DOC. The calculation of these characteristics is difficult for physicians who are attempting to interpret the related physiological implications and then use them clinically. Resting EEG data indicate spontaneous neural activity that is pertinent to the underlying brain state. In contrast, relevant characteristics generated from resting-state EEG may be useful for monitoring the brain status of DOC patients and contributing to care-related decisions. For that reason, EEG resting states are well-investigated to enhance our knowledge of the EEG features of DOC [13].

EEG resting states in BD: Another method, also one of the most promising EEG features in diagnosing BD, is the resting state. Resting-state EEG evaluations are designed to determine intrinsic brain activity not induced by a task. In an attempt to use EEG to diagnose BD, studies have been carried out [14-17].

D.J. Kim, et al. (2013) [14] employed disturbed resting state EEG synchronization to diagnose BD. It is hypothesized that a crucial aspect of BD is the disruption of functional connectivity, which represents disturbances of synchronization and oscillations within brain networks. During this project, the authors aimed to discover if individuals with BD have different synchronization or network characteristics in their resting EEG. In another study, resting EEG was once again utilized to distinguish between individuals with first-episode SCH, bipolar psychosis, and their first-degree relatives [15]. The researchers also employed resting EEG methods to investigate whether SCH and bipolar patients suffer from altered cortical functional networks [16]. Last, but not least, researchers also examined the relationships between cortical network indices and psychiatric, clinical, or cognitive measures to broaden current knowledge about both brain disorders.

Additionally, to differentiate between the following psychotic disorders SCH, BD and methamphetamine-induced psychotic disorder, F.M. Howells, et al. (2018) [17] used electroencephalographic delta/alpha frequency activity. Regarding their methodology, EEG was recorded under three different testing conditions: resting eyes open, resting eyes closed, and while performing cognitive tasks (visual continuous performance task). From those aforementioned studies, EEG data were extracted and processed before presenting the results. The EEG is a system that measures the frequency of brain waves. Generally, the raw EEG is described in terms of frequency bands: delta, alpha, gamma, and theta.

- For *delta*, when compared to multiple personality disorder (MPD) for the right hemisphere, bipolar patients exhibited lower delta/alpha frequency activity in resting eyes closed. However, when compared to HCs, bipolar patients displayed higher delta/alpha frequency activity during resting eyes opened [17].

- For *alpha*, BD patients exhibited a decrease in mean synchronization [13]. Also, in another study, there was a reduction in alpha activity in BD patients and reduced peak alpha frequencies [15].

- For *gamma*, gamma frequency band activities increased in bipolar patients when compared to first-episode SCH patients [15].

- For *theta*, theta frequency band activities increased in bipolar patients when compared to first-episode SCH patients [15]. Table 3 below summarizes the main findings from the aforementioned research.

Table 3. A brief summary of brain wave changes in BD patients compared to other psychiatric conditions.

Brain wavebands	Frequency range	Main findings	References
Alpha	8-12 Hz	Patients with BD demonstrated a reduction in mean synchronization. In addition, there was a decrease in alpha activity and peak alpha frequencies in BD patients.	[14, 15]
Gamma	>30 Hz	Gamma frequency band activities increased in BD patients when compared to first-episode SCH patients.	[15]
Theta	4-8 Hz	Theta frequency band activities increased in BD patients when compared to first-episode SCH patients.	[15]
Delta	0.5-4 Hz	In contrast to individuals with MPD for the right hemisphere, bipolar patients displayed decreased delta/alpha frequency activity in the resting/eyes closed state. However, compared to HCs, bipolar patients exhibited more delta/alpha frequency activity during eyes-open rest compared to CHs.	[17]

Other EEG features

Qualitative EEG (qEEG) is well-known as an optimal diagnostic tool in psychiatric diagnosis. With that in mind, the following study was carried out by comparing the differences and similarities between women with attention deficit hyperactivity disorder (ADHD), women with BD, and female HCs using qEEG [18]. In other words, they examined the similarities in EEG spectral power abnormalities during rest and cognitive function between women with ADHD and women with BD. The researchers discovered that during resting state conditions, the post-hoc tests displayed significantly higher absolute theta power in the ADHD group compared to HCs, but not during the Cue (CPT-OX). Their statistical technique also demonstrated that the BD group had significantly higher absolute theta power than the HCs, although not during the Cue (CPT-OX). Finally, during resting state or CPT-OX, no significant changes in absolute theta power between the ADHD and BD groups were found. While HCs demonstrated a task-related increase in absolute theta activity from resting to cognitive task, neither the BD nor the ADHD groups showed any significant changes. These findings might indicate evidence for commonalities in brain dysfunction between ADHD and BD. In both illnesses, absolute theta power may also serve as a marker of neurobiological processes.

Domain analysis, state-of-the-art techniques, and neural networks: A. Khaleghi, et al. (2015) [19] wants to utilize various domain analyses, state-of-the-art methodologies, and neural networks to classify the EEG signal of adolescents with BD I and BD II. Four alternative feature selection methods: mutual information maximization (MIM), conditional mutual information maximization (CMIM), fast correlation-based filter (FCBF), and double input symmetrical relevance (DISR) were used to determine the most discriminative features. Finally, for each feature selection technique, the extracted features were fed into a multi-layer perceptron (MLP) neural network as a classifier, and the system's performance was calculated. For the first time, the researchers used quantitative EEG processing techniques to classify BD subtypes. It was discovered that the PSD (power spectrum density) of the F3 and F4 channels of BD I and BD II were almost identical, although the spectrograms varied noticeably. As a result, spectrum-based features were more effective for distinguishing sub-types. The results demonstrate that combining DISR with MLP yields the greatest accuracy of 91.83%, which is acceptable for a medical diagnostic system. Furthermore, the following order of best to the worst performance in four distinct feature selection algorithms was provided as follows: DISR > CMIM > MIM > FCBF (average accuracy rate for test data set: 91.83>89.67>86.33>84.61).

The error-related negativity (ERN) and event-related brain potential (ERP): Some other EEG features that captured the attention of neurologists are the ERN and ERP. As far as we know, ERN is an electrical measure believed to reflect changes in dopamine when individuals make errors while performing cognitive activities, while ERP is defined as the brain's measurable reaction to a sensory, cognitive, or motor event. A study recorded EEG data from 16 patients with BD (euthymic state) and 14 matched HCs while executing a speeded two-choice reaction-time paradigm (flanker task) while EEG measurements were obtained to explain lower performance monitoring in BD using EEG signals [20]. The two groups' behavioural and ERP measures were then compared. As a result, S. Kim, et al. (2020) [16] found that, despite being euthymic, individuals with BD suffered more depressive symptoms than CHs. While no behavioural abnormalities were detected, when residual mood effects were considered, individuals with BD had lower ERN amplitudes than CHs. By observing lower ERN amplitudes, the researchers concluded that the reduction in ERN values in the BD group represented less performance monitoring that can expand our current knowledge of executive functioning in BD.

EEG power, cordance, and coherence: Researchers utilized EEG power, cordance, and coherence differences between unipolar and bipolar depression in this study [20]. A total of 25 bipolar and 56 unipolar depression patients were enrolled in the research. In addition to the resting state EEG, sociodemographic and clinical variables were obtained. When parametric assumptions were satisfied, data was examined using multivariate and repeated analyses of variance. No variations in EEG absolute power or frontal asymmetry indices were found between UD and BD in the research [18]. In terms of cordance, there were significant group differences in right theta cordance values ($p=0.031$). In terms of coherence, BD showed significantly higher central-temporal theta ($p=0.003$), parietal-temporal alpha ($p=0.007$), and theta ($p=0.001$) coherence than UD patients. Finally, the right frontal-central ($p=0.007$) and central inter-hemispheric ($p=0.019$) regions of the brain showed weaker alpha coherence in BD.

EEG entropy: As far as we know, EEG entropy is an EEG features that applies the idea of entropy to time series like EEG to provide a means to measure, in a statistical sense, the level of uncertainty or unpredictability in the pattern. The goal of this recent study [21] was to investigate if a deficit in EEG entropy might be applied as a biomarker for BD and SCH patients with impaired function. The researchers examined EEG spectral entropy modulation during a P300 task in 79 SCH patients (31 first episodes), 29 BD, and 48 HCs. Then, they performed a 3-tone auditory oddball task (P300 task), which is a well-established cognitive activity and event-related potential with a known spatial distribution. Meanwhile, C. Tas, et al. (2015) [22] discovered that patients with chronic or first-episode SCH and patients with BD had substantial spectral entropy modulation impairments with task performance, despite no significant pre-stimulus spectral entropy variations. MRI results also indicated the structural connectivity values were unrelated to the modulation of spectral entropy. Finally, the abnormalities were independent of treatment dosages, and there was no difference in spectral entropy modulation between individuals receiving antipsychotics, lithium, benzodiazepines, or antidepressants. As a result, in our review, Fig. 4 below illustrates important information of EEG features in bipolar diagnosis.

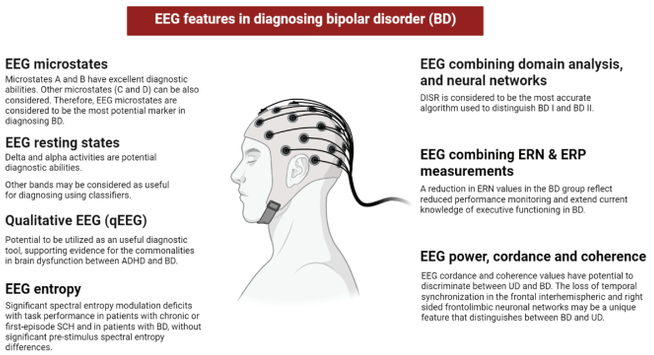

Fig. 4. A summary of EEG features in diagnosing BD.

Conclusions

In conclusion, this review presented a systematic mapping of EEG BD biomarkers, as well as a number of recent research works each with a brief explanation and comparison as well as a discussion of their state-of-the-art achievements. In this review, we categorized potential biomarkers into seven categories and concluded that the microstate features in EEG results would be the most potential marker in diagnosing BD because of the abnormal presence of microstate B in EEG topography. Additionally, the abnormalities in delta and alpha signals from EEG resting states were considered to be potential markers for diagnosing BD. Moreover, using other EEG features such as qualitative EEG (qEEG), EEG combining domain analysis and neural networks, EEG combining ERN and ERP measurements, EEG power, cordance and coherence, and EEG entropy could also potentially broaden our understanding of mental health problems like BD.

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COMPETING INTERESTS

The authors declare that there is no conflict of interest regarding the publication of this article.

REFERENCES

[1] I. Grand, M. Berk, B. Birmahe, E. Vieta (2016), "Bipolar disorder", *The Lancet*, **387(10027)**, pp.1561-1572.

[2] https://nami.org/About-Mental-Illness/Mental-Health-Conditions/Bipolar-Disorder.

[3] M. Sanches, I.E. Bauer, J.F. Galvez, G.B.Z. Soares, J.C. Soares (2015), "The management of cognitive impairment in bipolar disorder: Current status and perspectives", *American Journal of Therapeutics*, **22(6)**, pp.477-486.

[4] R. Degabriele, J. Lagopoulos (2009), "A review of EEG and ERP studies in bipolar disorder", *Acta Neuropsychiatrica*, **21(2)**, pp.58-66.

[5] B. Murray, et al. (2020), "Chronobiologic assessment methods for bipolar disorders: Current research protocols and clinical applications", *Bipolar Disorders Special Issue*, The 22nd Annual ISBD Conference, **22(1)**, pp.41-42.

[6] M. Vrabie, et al. (2015), "Cognitive impairment in manic bipolar patients: Important, understated, significant aspects", *Annals of General Psychiatry*, **14(1)**, pp.1-10.

[7] S. Gruber, K. Rathgeber, P. Bräunig, S. Gauggel (2007), "Stability and course of neuropsychological deficits in manic and depressed bipolar patients compared to patients with major depression", *Journal of Affective Disorders*, **104(1-3)**, pp.61-71.

[8] R.E. Kelly, W. Mansell, A.M. Wood, Y. Alatiq, A. Dodd, R. Searson (2011), "Extreme positive and negative appraisals of activated states interact to discriminate bipolar disorder from unipolar depression and non-clinical controls", *Journal of Affective Disorders*, **134(1-3)**, pp.438-443.

[9] H. Dinc, N.E. Boyacioglu, N.K. Ozcan, S. Enginkaya (2019), "Reproductive and sexual health in women with bipolar disorder: A comparative study", *Dusunen Adam the Journal of Psychiatry and Neurological Sciences*, **32**, pp.23-32.

[10] E. Marengo, et al. (2015), "Sexual risk behaviors among women with bipolar disorder", *Psychiatry Res.*, **230(3)**, pp.835-838.

[11] F. Wang, K. Hujjaree, X. Wang (2021), "Electroencephalographic microstates in schizophrenia and bipolar disorder", *Frontiers in Psychiatry*, **12**, DOI: 10.3389/fpsyt.2021.638722.

[12] M.I. Tomescu, et al. (2014), "Deviant dynamics of EEG resting state pattern in 22q11. 2 deletion syndrome adolescents: A vulnerability marker of schizophrenia?", *Schizophrenia Research*, **157(1-3)**, pp.175-181.

[13] F. Vellante, et al. (2020), "Euthymic bipolar disorder patients and EEG microstates: A neural signature of their abnormal self experience?", *Journal of Affective Disorders*, **272**, pp.326-334.

[14] D.J. Kim, et al. (2013), "Disturbed resting state EEG synchronization in bipolar disorder: A graph-theoretic analysis", *NeuroImage: Clinical*, **22(2)**, pp.414-423.

[15] B.A. Clementz, S.R. Sponheim, W.G. Iacono, M. Beiser (1994), "Resting EEG in first-episode schizophrenia patients, bipolar psychosis patients, and their first-degree relatives", *Psychophysiology*, **31(5)**, pp.486-494.

[16] S. Kim, et al. (2020), "Altered cortical functional networks in patients with schizophrenia and bipolar disorder: A resting-state electroencephalographic study", *Frontiers in Psychiatry*, **11(661)**, DOI: 10.3389/fpsyt.2020.00661.

[17] F.M. Howells, et al. (2018), "Electroencephalographic delta/alpha frequency activity differentiates psychotic disorders: A study of schizophrenia, bipolar disorder and methamphetamine-induced psychotic disorder", *Translational Psychiatry*, **8(1)**, pp.1-11.

[18] A.S. Rommel, et al. (2016), "Commonalities in EEG spectral power abnormalities between women with ADHD and women with bipolar disorder during rest and cognitive performance", *Brain Topography*, **29(6)**, pp.856-866.

[19] A. Khaleghi, et al. (2015), "EEG classification of adolescents with type I and type II of bipolar disorder", *Australasian Physical and Engineering Sciences in Medicine*, **38(4)**, pp.551-559.

[20] A.M. Morsel, M. Morrens, A. Temmerman, B. Sabbe, E.R. Bruijn (2014), "Electrophysiological (EEG) evidence for reduced performance monitoring in euthymic bipolar disorder", *Bipolar Disorders*, **16(8)**, pp.820-829.

[21] V. Molina, et al. (2020), "Deficits of entropy modulation of the EEG: A biomarker for altered function in schizophrenia and bipolar disorder?", *Journal of Psychiatry and Neuroscience*, **45(5)**, pp.322-333.

[22] C. Tas, et al. (2015), "EEG power, cordance and coherence differences between unipolar and bipolar depression", *Journal of Affective Disorders*, **172**, pp.184-190.